REMARKS

Reconsideration and allowance are requested.

The amendments to the claims find support throughout the originally filed disclosure and, thus, do not introduce new matter. The cancellation of claims 17-18 directed to UOG-1 protein is without prejudice to prosecuting the subject matter of those claims in a subsequent patent application.

Claims 4-10 are pending in this application.

Claims 4-10 and 17-18 were rejected under 35 U.S.C. 112, first paragraph, as allegedly "not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention". Applicant traverses.

On page 2, lines 12-13 of the Office Action (Paper No. 31), it is alleged that the claimed invention is not enabled because "there is no evidence of record that this DNA sequence encodes a biologically useful protein possessing any particular properties". Applicant submits that this is not the proper standard for patentability under Section 112, first paragraph, as the biological function of a protein is only one potential use for the claimed invention.

The specification states on page 12, lines 20-23, "one potential use for GDF-1 as a diagnostic tool is as a specific

marker for the presence of tumors arising from cell types that normally express GDF-1". The skilled artisan would understand that this can be generalized to the use of GDF-1 as a lineage marker for normal tissues as well (see temporal- and tissue-specific expression of GDF-1 discussed on pages 23-24 of the specification).

Figure 6 shows that different GDF-1 transcripts could be used to determine a cell's embryonic stage. Thus, detecting the presence of GDF-1 would be valuable in determining the action of growth and differentiation factors on the developing embryo or in cell culture.

Figure 7 shows that in adult tissues, GDF-1 was expressed almost exclusively in the brain, although GDF-1 was also detected in the adrenal gland, ovary, and oviduct. Thus, in addition to use of GDF-1 as a marker for a cell's stage of embryonic development, restriction of GDF-1 expression to particular adult tissues would be valuable in determining the tissue of origin for a cell.

Detection of GDF-1 expression is not limited to Northern blot analysis as shown in Figures 6-8. The specification describes the generation of specific antibodies to GDF-1 protein and their use in Western blot analysis (see Example 5 on pages 24-25 of the specification). The skilled artisan would recognize that such techniques are known in the art (page 12, lines 3-7 of the specification), and that detection

of protein to determine temporal- or tissue-specific expression of GDF-1 would be an alternative to detection of RNA. Thus, GDF-1 protein would be useful in developing a specific antibody to GDF-1 antigen.

A rejection based on an alleged lack of enablement requires that evidence, or a reason, be provided by the Examiner to substantiate an assertion that the objective truth contained in the disclosure is doubted. M.P.E.P. 2164.01. This burden of persuasion has been described by the Court:

> "[I]t is incumbent on the Patent Office, whenever a rejection on this basis is made, to explain why it doubts the truth or accuracy of any statement in a supporting disclosure and to back up assertions of its own with acceptable evidence or reasoning which is inconsistent with the contested statement. Otherwise, there would be no need for the applicant to go to the trouble and expense of supporting his presumptively accurate disclosure."

In re Marzocchi, 169 U.S.P.Q. 367, 370 (C.C.P.A. 1971).

As shown by citation to the present specification and the understanding that a skilled artisan would gain from reading that specification, the claimed invention would find use in determining a cell's stage of development and/or its tissue of origin. Such determination would find application in any situation in which a mixture of cell types is suspected. For example, determining whether a tumor arose from a cell of the surrounding tissue (i.e., a primary tumor) or was a metastasis from a different tissue would have diagnostic and treatment consequences. For cultures of undifferentiated cells, the

action of growth or differentiation factors on the culture may be determined by detection of GDF-1. For determining the developmental stage of an embryo, determination of GDF-1 would provide a marker of age.

As discussed above, the use of antibody binding to GDF-1 protein provides an art-recognized alternative to nucleic acid hybridization. Such an antibody would be generated using GDF-1 protein, preferably produced recombinantly, as described in the specification.

If this rejection is maintained, and in accordance with In re Marzocchi, the Examiner is requested to provide evidence or a reason to substantiate doubting the objective truth that GDF-1 transcript and/or protein would be useful in determining the lineage of a cell, or that such a determination would not have "practical utility".

Finally, a similar argument could be made that a therapeutic use for UOG-1 protein is not required to satisfy the enablement requirement of Section 112, however, the above rejection is moot with respect to claims 18-19 as those claims have been canceled.

Claims 8-9 and 18 were rejected under 35 U.S.C. 112, second paragraph, as allegedly indefinite. Applicant traverses. Figures 2, 11A and 11B clearly show an amino acid sequence which is GDF-1 and claims 8-9 recite that the intended sequence is that of GDF-1. Similarly, claim 18 could

be amended to recite "the UOG-1 amino acid sequence" if the above rejection were not moot after cancellation of the claim.

For the above reasons, applicant requests withdrawal of the objections to the specification and the rejections of the claims under Section 112.

Claims 4-10 were rejected under 35 U.S.C. 102(e) as being allegedly anticipated by Derynck et al. (U.S. Pat. No. 4,886,747). Applicant traverses.

The Examiner appears to take the position that applicant's observation that GDF-1 belongs to the TGF β superfamily allows one to conclude that any other member of the superfamily would anticipate the claimed invention. This is not correct as the specification compares the amino acid sequences of different members of the TGF β superfamily in Figure 3 to show that GDF-1 is a novel member of the superfamily. Thus, TGFβ1, TGFβ2 and TGFβ3 cannot anticipate GDF-1 of the present invention.

The phrases "unique portion" and "functionally equivalent variation" appear in the specification but are not recited in the claims. In proper context, the definition of "unique portion" given on page 9 of the specification means the nucleotide or amino acid sequence has a certain length, and is unique with respect to other members of the TGFβ superfamily. Thus, any portion of sequence shared by GDF-1 and another member of the TGFβ superfamily could not be unique.

For the above reasons, applicant requests withdrawal of the rejection of the claims under Section 102.

Having responded to the objections and rejections in the pending Office Action, applicant submits the amended claims are in condition for allowance and a Notice to that effect is requested. The Examiner is invited to contact the undersigned if further information is needed.

Respectfully submitted,

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